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Radical Ring Closures of 4-Isocyanato Carbon-Centered Radicals

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Abstract: The 2-(2-isocyanatophenyl)ethyl radical was generated from the corresponding bromide with tributyltin and tris(trimethylsilyl)silyl radicals and shown to ring close in the 6-*endo*-mode to afford 3,4-dihydro-1*H*-quinolin-2-one as the major product. Cyclization in the 5-*exo*-mode to produce 2,3-dihydroindole-1-carbaldehyde, after hydrogen abstraction, was a minor reaction. Rate constants for the two processes were estimated and compared with reaction enthalpies computed by the DFT method.

Cyclization of ω-isocyanato-C-centered radicals is potentially an important route for the preparation of various nitrogen heterocycles. Two main modes of ring closure can be envisaged for this asymmetric heterocumulene. For example, radical **1** could cyclize at the central C-atom, in the *endo* mode, to afford acylaminyl radical **2** or at the *N*-terminus to produce aminoacyl radical **3** (Scheme 1). Literature precedents are sparse.[1] The 2-(isocyanatocarbonyl)ethyl radical cyclized rapidly and reversibly to the succinimidyl radical.[2,3] Similarly, the 3-(isocyanatocarbonyl)propyl radical **4** afforded the glutarimidyl radical **5** via a 6-*endo*-type process.[3]

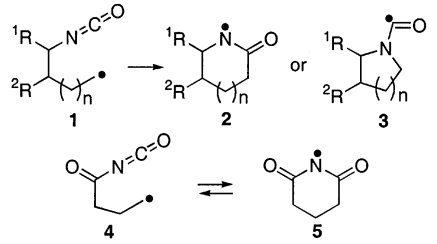
Photolysis of biphenyl-2-isocyanate gave the ring-closed carbazole and phenanthridone as the major products.[4] It is doubtful, however, if this reaction involved a radical mechanism; an excited state of the isocyanate and 2-biphenyl nitrene are more likely intermediates. Radical cyclization onto the allene moiety has been observed to occur in either or both modes, depending on the substitution pattern.[5,6] Information about intermolecular radical additions to organic isocyanates is also scarce, although hydrogen atoms generally prefer to add to the central C-atom.[7] We report here a study of the ring-closure reactions of the 2-(2-isocyanatophenyl)ethyl and 4-isocyanatobutyl radicals.

Amino-alcohol **8** (Scheme 2) appeared to be a suitable intermediate from which precursors of the 2-(2-isocyanatophenyl)ethyl radical might be made. It was obtained by treatment of 2-nitrophenol with formaldehyde and sodium phenoxide,[8] to give nitro-alcohol **7**, which was smoothly reduced to the desired amino-alcohol **8**. Attempts to convert the hydroxyl group of **8** to a bromine atom either with PBr_3 or via the mesylate and LiBr, or by use of CBr_4/PPh_3, were unsuccessful. The amino group of **8** was therefore Boc protected giving **9** and the protected compound was satisfactorily brominated with PBr_3 to afford **10**. However, attempts to deprotect **10** led to mixtures in which 2,3-dihydroindole **11** was a major component. Evidently the 2-(2-bromoethyl)phenylamine underwent an intramolecular nucleophilic substitution that closed the ring to produce **11**.

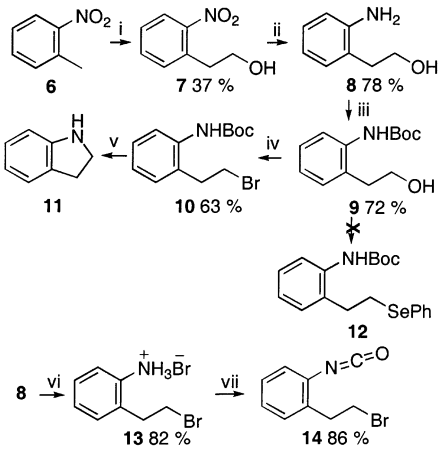
In view of this, attempts were made to prepare the phenyl selenide **12** as a radical precursor not readily susceptible to nucleophilic displacement. However, treatment of **9** with PhSeCN led only to intractable mixtures. Eventually we found that refluxing amino-alcohol **8** in 48% aq HBr gave the hydrobromide salt **13** in high yield. Not only did this provide a precursor to the isocyanate, but simultaneously protected the amino group and prevented nucleophilic ring closure. Isocyanate **14** was successfully made by treatment of **13** with phosgene.

Isocyanate **14** was reacted with tributyltin hydride by using thermal initiation with AIBN, photochemical initiation, and conditions of slow organotin addition. The products identified were similar in each case and are set out in Scheme 3. The main product, 3,4-dihydro-1*H*-quinolin-2-one **19**, was evidently formed by 6-*endo*-

SCHEME 1



SCHEME 2[a]



[a] Reagents and conditions: (i) $(CH_2O)_n$, PhONa, DMSO, 1 h, 65 °C. (ii) $CaCl_2$/Zn. (iii) DBD, $NaHCO_3$, dioxane. (iv) PBr_3, PyH, hexane. (v) HCl. (vi) HBr, H_2O, 4 h. (vii) $COCl_2$, PhMe, 120 °C.

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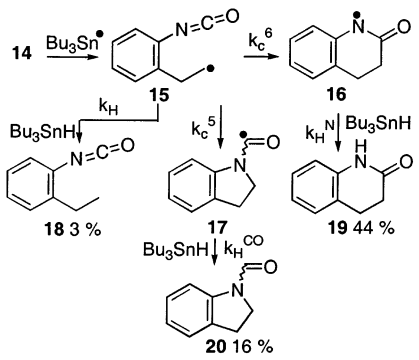
SCHEME 3



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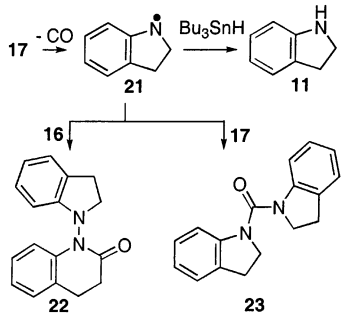

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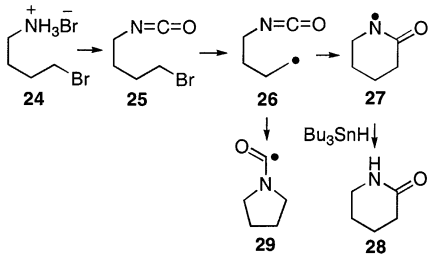

cyclization of radical **15** to give acylaminyl radical **16** that abstracted an H-atom from the tin hydride.[9] 2,3-Dihydroindole-1-carbaldehyde **20** (2 conformers about the N−C(O) bond, ratio 3:1) was formed by 5-*exo*-cyclization at the N-terminus of the isocyanate group. A small amount of the direct reduction product **18** was also obtained.

Analysis of the product mixtures by GC-MS showed that small amounts of dihydroindole **11** and the two cross-coupled products **22** and **23** (ratio 1.7:1) were also formed. The dihydroindole might have been formed by hydrolysis of the isocyanate to give 2-(2-bromoethyl)-aniline that subsequently underwent intramolecular nucleophilic ring closure. However, the presence of the coupled products **22** and **23** is good evidence that dihydroindolyl radicals **21** were generated by decarbonylation of **17** and hence there was no necessity to invoke the hydrolysis process (Scheme 4).

The yields from a photochemical reaction of **14** with Bu_3SnH (1 equiv) at 30 °C (Scheme 3) showed that 6-*endo*-cyclization at the central C-atom predominated over 5-*exo*-cyclization at the terminal N-atom by a factor of 2.8. Reactions with 0.5 and 2 equiv of Bu_3SnH gave similar **19**/**20** ratios and this indicated that the ring closures were not reversible at this temperature. A general, integrated, rate equation applicable for such cyclizations, based on a mechanism analogous to that of Scheme 3, has been published.[10] However, use of this would be over-stretching the limited data and hence approximate expressions, $k_c^6/k_H = [Bu_3SnH][\mathbf{19}/\mathbf{18}]$ and $k_c^5/k_H = [Bu_3SnH][\mathbf{20}/\mathbf{18}]$, with a mean value of the tin hydride concentration (0.11 M), have been used. From the experimental data $k_c^6/k_H(30\ °C) = 1.6$ M and $k_c^5/k_H(30\ °C) = 0.6$ M. The k_H constant refers to H-abstraction from Bu_3SnH by a primary C-centered radical and hence the data of Ingold and co-workers are appropriate, i.e., $\log(k_H/M^{-1}\ s^{-1}) = 9.1 - 3.7/\theta$.[11,12] Hence $k_c^6(30\ °C) = 4.2 \times 10^6$ and $k_c^5(30\ °C) = 1.5 \times 10^6\ s^{-1}$. These rate constants are about an order of magnitude greater than k_c^5 for the archetype unsubstituted hex-5-enyl radical ($2.3 \times 10^5\ s^{-1}$ at 25 °C).[9] Rate data are not available for cyclizations of all-carbon close structural analogues of **15**. However, the 6-*endo* process of **15** is undoubtedly enhanced by the resonance stabilization in radical **16**. Similar benzyl-type resonance stabilization in for example 6,6-diphenylhex-5-enyl cyclization [$k_c(25\ °C) = 5 \times 10^7\ s^{-1}$][12] and the 6-phenyl-1-aza-analogue[13] increases the rate constants by 1 to 2 orders of magnitude. Both cyclizations of **15** are probably also favored by conformational constraint. Cyclization of **15** is a rapid process, partly due to special structural features; ring closure onto isocyanate in general should not be viewed as inherently faster than that for all-carbon analogues.

In an analogous reaction of **14** mediated by tris-(trimethylsilyl)silane (TTMSS), and initiated thermally at 103 °C with 1,1′-bis(cyclohexanecarbonitrile), conversion of **14** was low (26%). However, the same three products, i.e., **18**, **19**, and **20** were obtained in yields of 1%, 18%, and 1.3%, respectively. In this case the cyclization was much more regioselective, the [**19**]:[**20**] ratio being 14:1. This could indicate that 5-*exo*-cyclization to **17** was reversible at the higher temperature of the TTMSS reaction, whereas the 6-*endo* process, which gave the resonance stabilized radical **16**, was not. The system would be under thermodynamic control at 103 °C. Because TTMSS is a slower H-atom donor than Bu_3SnH, more product would build up via the irreversible reaction channel leading to **19** with the Si-hydride as compared with the Sn-hydride.[14]

From the experimental data, cyclization rate constants can be estimated as described above. Assuming irreversible cyclizations and using an average [TTMSS] (0.19 M) gave $k_c^6/k_H^{Si}(103\ °C) = 3$ M and $k_c^5/k_H^{Si}(103\ °C) = 0.2$ M. Using the k_H^{Si} value determined for C-centered radicals [$\log(k_H^{Si}/M^{-1}\ s^{-1}) = 8.9 - 4.5/\theta$][15] results in $k_c^6(103\ °C) = 6 \times 10^6$ and $k_c^5(103\ °C) = 0.4 \times 10^6\ s^{-1}$. This value for k_c^6 agrees fairly well with the result from the tin hydride experiment (above), taking the higher temperature into

(9) Alternatively, the cyclization might be considered as 6-*exo*. H-atom abstraction by the O-centered mesomer of **16** might afford an iminol that would tautomerize to **19**.

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TABLE 1. Enthalpies of Cyclization Reactions (kcal mol^{-1}) Computed by Using the Ab Initio DFT UB3LYP Method[a]

cyclization	method/basis set	reaction enthalpy
15 → **16** (6-*endo*)	UB3LYP/6-31G(d,p)	−4.4
	UB3LYP/6-311+G(d,p)	−13.8
15 → **17** (5-*exo*)	UB3LYP/6-31G(d,p)	+3.6
	UB3LYP/6-311+G(d,p)	−6.4
26 → **27** (6-*endo*)	UB3LYP/6-31G(d,p)	−5.8
	UB3LYP/6-311+G(d,p)	−2.9
26 → **29** (5-*exo*)	UB3LYP/6-31G(d,p)	−8.4
	UB3LYP/6-311+G(d,p)	−6.5

[a] All geometries fully optimized at the stated level, energies corrected for zero-point vibrations and for vibrational effects to 298 K.

account. The lower magnitude of k_c^5, in comparison with the tin result, suggests reversibility plays a part. If the 5-*exo*-process is reversible, more complex rate equations will be needed to evaluate k_c^5 at the higher temperature. An attempt to use 1-ethylpiperidine hypophosphite (EPHP) in place of Bu_3SnH[16] was not successful and gave a complex mixture of products.

1-Bromo-4-isocyanatobutane **25** was prepared from the hydrobromide salt **24**, obtained on treatment of 4-aminobutanol with aq HBr, using similar methodology to that outlined above. However, clean reactions of **25** with Bu_3SnH were not obtained. This was probably because the organostannane reacted with the isocyanate group, as found for carbonylisocyanates.[3] The GC-MS showed *n*-butylisocyanate, piperidine-2-one (**28**), and 1-pyrrolidine-carboxaldehyde (**29**-H) in low yields, together with several unidentified components containing pyrrolidine and piperidine rings.

Reduction of isocyanate **24** with TTMSS was also investigated, but conversion was low in experiments at 83 °C, and only traces of piperidinone **28** were detected. Both cyclization modes were evidently operative in these reactions but, in view of their incomplete and defective character, conclusions about the regioselectivity would be unsafe.

The thermochemistry of the two cyclization modes was computed by using DFT methods implemented with the Gaussian 98 program package.[17] The enthalpies of 6-*endo*- and 5-*exo*-cyclizations for radicals **14** and **26**, computed with two different basis sets, are given in Table 1.

For radical **15**, computations with the larger, more reliable basis set predicted both ring closure modes to be exothermic, but found a clear preference for the 6-*endo* process, in good agreement with experiment. As might be expected, in view of the absence of aromatic resonance stabilization in radical **27**, the computations predicted a preference for 5-*exo* cyclization for the 4-isocyanatobutyl radical **26**. Furthermore, with the larger basis set, cyclization was predicted to be more difficult, from a thermodynamic standpoint, for radical **26** compared to **15**.

Cyclization of the 2-(2-isocyanatophenyl)ethyl radical took place in both 6-*endo*- and 5-*exo*-modes at rates that were faster that that of the hex-5-enyl radical. The thermodynamically more stable 3,4-dihydro-2-oxo-1*H*-quinolinyl radical was the major product. The selectivity of ring closure was moderate when Bu_3SnH was used to mediate the reactions but improved considerably with TTMSS. Results for the 4-isocyanatobutyl radical were less clear-cut but both cyclization modes again appeared to compete. From these results it may be concluded that 6-*endo*-cyclization of C-centered radicals onto isocyanates is sufficiently rapid for preparative purposes, provided the cyclized radical is stabilized by aromatic resonance delocalization. The regioselectivity for dihydroquinolinones can be improved by use of TTMSS and conditions that promote thermodynamic control. The method complements previous work on radical ring closures of aldimines[18] and azomethines.[19]

Experimental Section

General Methods. ^{1}H (300 and 500 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in deuteriochloroform with tetramethylsilane as an internal standard. *J* values are reported in hertz. EI mass spectra, and high-resolution mass spectra, were obtained with 70-eV ionization and CI spectra were obtained with isobutane as the target gas. GC-MS analyses were run with the MS instrument coupled to a GC fitted with a 25-m HP 17-capillary column (50% phenyl methyl silicone). IR spectra were recorded in Nujol or neat on an FT-IR spectrometer. Column chromatography was carried out on ICN silica gel (63-200, 60 Å). Previously reported reaction products were identified by spectral comparison. Ether is diethyl ether.

2-(2-Nitrophenyl)ethanol (7).[8] 2-Nitrotoluene (9.2 g, 67.0 mmol), sodium phenoxide (0.06 g, 0.56 mmol), paraformaldehyde (0.9 g of 95%), and dimethyl sulfoxide (20 mL) were heated for 1 h at 60−67 °C. The mixture was poured into water and extracted with ether. The combined extracts were washed with saturated sodium chloride solution. The organic phases were dried over magnesium sulfate and evaporated. A yellow oil (4.3 g, 37%) was obtained by Kugelrohr distillation at 140 °C/0.1 mmHg. ^{1}H NMR: δ_H 2.1 (1H, br s, OH), 3.10−3.25 (2H, m), 3.90−4.10 (2H, m), 7.20 (1H, s, ArH), 7.35−7.45 (1H, m, AH), 7.50−7.60 (1H, m, AH), 7.90−8.10 (1H, m, ArH). ^{13}C NMR: δ_C 35.90, 62.55, 124.63, 127.40, 132.60, 132.83, 133.65, 149.65. IR: 3365 cm^{-1} (ν_{OH}); 1525 and 1348 cm^{-1} (ν_{NO_2}).

2-(2-Aminophenyl)ethanol (8).[20] 2-(2-Nitrophenyl)ethanol (3 g, 18 mmol) was added dropwise to a flask containing calcium chloride (1.2 g, 12.0 mmol) and zinc powder (4 g, 180 mmol) in hot water (25 mL). The mixture was heated under reflux for 30 min. The zinc was filtered and washed and sodium carbonate (1.2 g, 12.0 mmol) was added to the filtrate. The salt was filtered and washed and the water was removed under vacuum. A mixture of sodium chloride and oil was obtained. The crude product was extracted with ether. The salt was filtered and the solvent was removed under vacuum. The title compound was obtained as a yellow oil after Kugelrohr distillation at 155 °C/0.1 mmHg (2 g, 78%). ^{1}H NMR: δ_H 2.55−2.70 (2H, m, CH_2), 3.25−3.35 (3H, s, NH_2 and OH), 3.70−3.90 (2H, m, CH_2), 6.60−

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6.80 (2H, m, ArH), 7.10−7.25 (2H, m, ArH). ^{13}C NMR: δ_C 34.65, 62.95, 116.20, 119.13, 124.44, 127.50, 130.43, 144.80. IR: 3366 cm^{-1} (ν_{OH}); 2878−2942, 1263 and 1044 cm^{-1} (ν_{C-NH_2}).

Hydrobromide of 1-(2-Bromoethyl)-2-aminobenzene (13). 2-(2-Aminophenyl)ethanol (0.24 g, 1.75 mmol) was dissolved in constant-boiling hydrobromic acid (20 mL, 48% in water) and refluxed for 4 h. The crystalline precipitate was filtered, washed with ice-cold hydrobromic acid, and dried in vacuo to yield the salt as a light gray solid (0.29 g, 82%). Mp 161 °C. ^{1}H NMR (D_2O): δ_H 2.82 (2H, t, CH_2, $^3J_{HH}$ = 10.6), 3.75 (2H, t, CH_2Br, $^3J_{HH}$ = 10.6), 4.70 (2H, s, NH_2), 7.20−7.40 (4H, m, ArH).

1-(2-Bromoethyl)-2-isocyanatobenzene (14). To a solution of the hydrobromide of 2-(2-bromoethyl)aniline in toluene (0.6 g, 21 mmol) was added, at 120 °C over 10 min, a solution of phosgene in toluene (5 mL of 20%). The solvent and excess of phosgene were removed in vacuo to give of the title compound (0.4 g, 86%). ^{1}H NMR: δ_H 3.20 (2H, t, CH_2, $^3J_{HH}$ = 7.6), 3.57 (2H, t, CH_2Br, $^3J_{HH}$ = 7.6), 7.10−7.45 (4H, m, ArH). ^{13}C NMR: δ_c 31.77, 35.99, 121.59, 124.90, 126.41, 126.74, 128.75, 131.00, 133.22. IR 2271.64 cm^{-1} (ν_{NCO}). Found C 47.82, H 3.57, N 6.20; C_9H_8NOBr requires C 47.49, H 3.38, N 6.98.

Photoinitiated Reaction of 1-(2-Bromoethyl)-2-isocyanatobenzene 14 with Tributyltin Hydride. A solution of **14** (0.1 g, 0.44 mmol) and tributyltin hydride (0.13 g, 0.44 mmol) in benzene (2 mL) was photolyzed in a quartz tube with light from a 400-W medium-pressure Hg lamp at ambient temperature (30 °C) for 3 h. The solution was degassed for 15 min before photolysis. The solution was chromatographed on neutral alumina eluting with hexane/ethyl acetate (1:1). Several preliminary fractions containing tin residues were obtained followed by a final fraction containing the products (0.05 g, 77%). The final fraction was examined by ^{1}H NMR, which showed the presence of 3,4-dihydro-1*H*-quinolin-2-one **19** (44%): δ_H 2.63 (1H, d, J = 7.4), 2.66 (1H, d, J = 5.9), 2.98 (2H, t, J = 7.6), 6.75 (1H, d, J = 7.9), 6.99 (1H, dd, J = 6.9, 8.5), 7.17 (2H, m), 8.02 (1H, br s). This spectrum was essentially the same as that reported in the literature,[21] 2,3-dihydroindole-1-carbaldehyde **20** (2 isomers, ratio 3:1). Major isomer (12%): δ_H 3.16 (2H, m), 4.08 (2H, t, J = 8.7), 7.05−7.4 (4H, m), 8.94 (1H, s). Minor isomer (4%): δ_H 3.24 (2H, m), 4.13 (2H, m), 8.53 (1H, s). The spectra were essentially identical with those reported in the literature[22] and 2-ethyl phenylisocyanate **18** (3%): δ_H 1.15 (3H, t, J = 7.5), 2.59 (2H, q, J = 7.5), 7.2−7.4 (4H, m). Several resonances due to minor unidentified components were also present. GC-MS: *Peak 271* (minor), 2,3-dihydro-1*H*-indole **11**, *m*/*z* (%) 118 (100), 91 (21), 65 (6), 59 (9) (library fit 988). *Peak 324*, 1-ethyl-2-isocyanatobenzene **18** *m*/*z* (%) 147 (49), 132 (100), 119 (26), 104 (8), 77 (21), 63 (7), 51 (15). *Peak 399*, 2,3-dihydroindole-1-carbaldehyde **20**, *m*/*z* (%) 147 (80), 118 (100), 91 (28), 65 (9), 51 (5) (library fit 990). *Peak 430*, 3,4-dihydro-1*H*-quinolin-2-one **19**, *m*/*z* (%) 147 (100), 128 (9), 118 (56), 104 (15), 92 (24), 78 (14), 63 (5), 59 (8) (library fit 990). *Peak 644* (minor), 1-(2,3-dihydroindol-1-yl)-3,4-dihydro-1*H*-quinolin-2-one **22**, *m*/*z* (%) 264 (63), 146 (100), 128 (45), 118 (30), 117 (15), 103 (5), 91 (24), 77 (13), 65(9). *Peak 659* (minor), bis(2,3-dihydroindol-1-yl)methanone **23**, *m*/*z* (%) 264 (65), 147 (6), 132 (10), 118 (100), 91 (15), 77 (7), 65 (3). Ratio of *644:659* was 1.7:1. Reactions of **14** with Bu_3SnH were also carried out with 0.5 and 2.0 equiv of the tin hydride and with slow addition of the latter to a toluene solution of **14**. GC analyses showed the same products were formed in each case. The **19**:**20** ratio was the same, to within the experimental error, but as expected, the proportion of **18** was reduced in the experiments with lower Bu_3SnH concentrations.

Photoinitiated Reaction of 1-(2-Bromoethyl)-2-isocyanatobenzene (14) with Tris(trimethylsilyl)silane. A solution of 1-(2-bromoethyl)-2-isocyanatobenzene (0.04 g, 0.18 mmol) and TTMSS (0.052 g, 0.21 mmol) in deuteriobenzene (1 mL) was heated at 103 °C with 1,1′-azobis(cyclohexanecarbonitrile) (4 mg) for 2 h. The ^{1}H NMR spectrum (500 MHz, C_6D_6) showed unreacted **14** (74%) (and TTMSS) together with 3,4-dihydro-1*H*-quinolin-2-one **19** (18%), 1-ethyl-2-isocyanatobenzene **18** (1%), and 2,3-dihydroindole-1-carbaldehyde **20** (1.3%). The chemical shifts of reactant **14** and the products were significantly different in C_6D_6 from $CDCl_3$. GC-MS: *Peak 10.6*, 1-ethyl-2-isocyanatobenzene **18**; *Peak 15.1*, 2,3-dihydroindole-1-carbaldehyde **20**; *Peak 15.6*, 3,4-dihydro-1*H*-quinolin-2-one **19**; and *Peak 23.1*, 1-(2,3-dihydroindol-1-yl)-3,4-dihydro-1*H*-quinolin-2-one **22**. TTMSS and other unidentified components (mostly Si compounds) were also observed.

4-Bromobutylamine, Hydrobromide Salt. 4-Aminobutan-1-ol (2 g, 22.4 mmol) was refluxed for 3 h in aqueous hydrobromic acid (48%). On cooling, the solvent was removed under vacuum, to afford 3.49 g (68%) of crude hydrobromide salt. δ_H 1.60−1.71 (2H, m), 1.78−1.83 (2H, m), 2.84−2.90 (2H, m), 3.36−3.40 (2H, m); δ_C 25.8, 29.2, 33.8, 39.1; $\nu_{NH_3^+}$ 1500 cm^{-1} and ν_{NH} = 3490 cm^{-1}. M$^+$ 233(1), 210(4), 194(5), 152(100), 135(8), 72(94). Found C 20.79, H 4.24, N 6.15; $C_4H_{11}NBr_2$ requires C 20.62, H 4.76, N 6.01.

1-Bromo-4-isocyanatobutane (25). The hydrobromide salt of 1-bromo-4-aminobutane (2.15 g, 9.2 mmol) in benzene (30 mL) was treated with phosgene (10 mL of 20% soln in toluene) at 120 °C for 15 min. The solvent was evaporated and the product was distilled at 120 °C/10 mmHg, lit.[23] 84−86 °C/12 mmHg, to yield the title compound (1.4 g, 89%): δ_H 1.78 (2H, quin, J = 7.0), 1.98 (2H, quin, J = 7.0), 3.38 (2H, t, J = 6.4), 3.44 (2H, t, J = 6.7); δ_C 30.0, 30.1, 34.0, 42.6, 123.2; ν_{NCO} = 2272 cm^{-1}. The NMR spectra showed contamination by about 9% benzyl bromide.

Photochemical Reactions of 1-Bromo-4-isocyanatobutane (25) with Tin and Silicon Hydrides. A solution of isocyanate **25** (0.1 g, 0.56 mmol) and tributyltin hydride (0.17 g, 0.56 mmol) in benzene (3 mL) was photolyzed in a quartz tube with light from a 400-W medium-pressure Hg lamp at ambient temperature (30 °C) for 3 h. The solution was degassed for 15 min before photolysis. GC-MS analysis showed the following components: *Peak 62*, *n*-butylisocyanate (library fit 947); *Peaks 262* and *277*, mixture of piperidine-2-one (**28**) (library fit 937) and 1-pyrrolidine-carboxaldehyde (**29-H**) (library fit 794); *Peak 438*, M$^+$ 168, $C_9H_{16}N_2O$ (probably dipyrrolidin-1-yl-methanone or 1-pyrrolidin-1-yl-piperidin-2-one); and *Peak 441*, M$^+$ 170, $C_9H_{18}N_2O$ together with several unidentified components. The ^{1}H NMR spectrum of the whole mixture indicated the expected resonances for the above components although with major overlaps of the multiplets. The experiment was repeated but with similar results.

Bromo-isocyanate **25** (20 mg, 0.1 mmol) and TTMSS (33 mg) with 1,1′-azobis(cyclohexanecarbonitrile) (3 mg) in deuteriobenzene (1 mL) were heated at 83 °C for 7 h. The ^{1}H NMR spectrum showed mainly unreacted starting materials. GC-MS analysis confirmed that conversion of the bromo-isocyanate was low, but showed a small amount of piperidine-2-one (**28**).

Computational Methods. Quantum chemical calculations were carried out for the 4-isocyanato radicals with the Gaussian 98W package.[15] Density functional theory, UB3LYP variant, was employed. The equilibrium geometries were fully optimized with respect to all geometric variables, no symmetry being assumed, with the 6-31G(d,p) and 6-311+G(d,p) basis sets. For the calculation of thermodynamic properties total energies were adjusted for zero-point vibrational energies and for thermal corrections to 298 K.

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Supporting Information Available: Gaussian 98 archive files, table of energies, and images of optimized structures for radicals **15**, **16**, **17**, **26**, **27**, and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

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